Amendments to the Specification

On page 1, please replace the title with the following:

~~Method~~<u>Microfluidic Device</u> for Controlling Sample Introduction in Microcolumn Separation Techniques and Sampling Device

On page 4, please replace the paragraph starting on line 1 with the following:

In a further preferred process step, immediately after the injection of the sample plug, the electrolyte buffer is allowed to advance into the supply channel and into the drain channel at the respective supply and drain ports for a time period, which amounts to at least the migration time of a slowest component within the sample plug from the supply port to the detector. Thus, the sample is pushed back into the respective supply and drain channels and substantially prevented from uncontrollably diffusing into the electrolyte buffer which is transported past the supply and drain ports. In addition the method allows ~~to~~<u>for</u> control <u>of</u> the sample composition within the electrolyte buffer.

On page 4, please replace the paragraph starting on line 10 with the following:

The sampling device according to the invention comprises an electrolyte channel, and a supply channel and a drain channel for the sample, which discharge into the electrolyte channel at respective supply and drain ports. The ports are arranged with respect to each other such[[,]] that a sample volume is geometrically defined. The supply and drain channels each are inclined to the electrolyte channel. Means are provided for electro-kinetically injecting a sample into the sample volume. The resistance to flow of the source and drain channels with respect to the electrolyte buffer is at least about 5% lower than the respective resistance to flow of the electrolyte channel. Preferred variants of the method according to the invention and preferred embodiments of the sampling device according to the invention are subject of the respective dependent claims.

On page 5, please replace the paragraph starting on line 36 with the following:

In Fig. 3, a first exemplary embodiment of the sampling device is shown. It comprises a capillary channel piece 22, which on one end is connected to a capillary channel communicating with the reservoir R for the electrolyte buffer and in a longitudinal direction on the other end with a capillary channel where the electrophoretic separation of the sample takes place, and which leads to the detector(s) and in further consequence to the waste receptacle(s) W. The sampling device further comprises a supply channel 23, which communicates with a source receptacle S for the sample, and a drain channel 24 which leads to a drain receptacle D. The source channel 23 and the drain channel 24 are inclined to the longitudinal extension of the channel piece 22, preferably they are arranged about perpendicular such, that together with the channel piece 22 they form a double T structure, as shown in the drawing. The source channel S and the drain channel D each discharge into the channel piece 22 at respective supply and drain ports 25, 26. According to the drawing in Fig. 3 the supply port 25 and the drain port 26 are spaced apart from each other longitudinally at the channel piece 22 such, that a sample volume 27 is geometrically defined as will be explained in more detail hereinafter. It is to be understood, that the drain channel 24 can be arranged in direct longitudinal extension of the source channel 23 such, that the supply and drain ports 25, 26 are situated opposite each other. In that case, the channels of the sampling device have no double T structure, but they are arranged in the form of an ordinary crossing.

On page 6, please replace the paragraph starting on line 17 with the following:

As already mentioned before the transport of the fluids, i.e. the electrolyte buffer and the sample, is accomplished with electric fields, which are a result of different electric potentials at the reservoir R and the waste receptacle W for the electrolyte buffer, and the respective source receptacle S and the drain receptacle D for the sample. By applying, for example, a positive electric potential to the reservoir R and a negative electric potential to the waste receptacle, the electrolyte buffer is electro-kinetically transported from the reservoir R through the capillary channel system to the waste receptacle W. In order to introduce the sample into the channel piece 22, for example, the source receptacle S for the sample is maintained at a positive potential and the drain receptacle D is kept on a negative potential. In the resulting electric field the sample is transported electro-kinetically from the source receptacle S to the drain receptacle D. The direction of flow is indicated in Fig. 3 by the arrows S, V, and D. By this measure, a part 27 of the channel piece 22, which is delimited by the supply port 25 on the one end and by the drain port 26 on the other end is filled with sample. Thus, the sample-filled part 27 of the channel piece of the sampling device 3 defines the volume of the electro-kinetically injected sample plug, which is indicated by the hatchings in Fig. 3. In other words, the volume 27 of the sample plug is geometrically delimited by the spaced apart supply and drain ports 25 and 26. In the ~~aforemantioned~~aforementioned case that the supply and drain ports are arranged opposite each other, such that the channel piece 22 and the supply and drain channels 23, 24 form an ordinary crossing, the size and volume of the intersection determines the sample volume. Thus, in that case, the sample volume is only defined by the cross-sections of the respective channels 22, 23, 24.

On page 8, please replace the paragraph starting on line 35 with the following:
Another approach to allow an advancement of the electrolyte buffer into the supply and drain channels 3, 4 is depicted in Fig. 4. The construction of the depicted sampling device 3 basically corresponds to the one depicted in Fig. 3. It comprises a channel piece 12 with two side channels 13, 14. The side channels are inclined to the longitudinal extension of the channel piece 12 at an angle that amounts to from about 5 degrees to about 175 degrees; however, preferably they are arranged about perpendicular with respect to the channel piece 12. The side channels are a supply channel 13 and a drain channel 14, which discharge into the channel piece 12 at respective supply and drain ports 15, 16. Preferably the supply port 15 and the drain port 16 are spaced apart from each other at the channel piece 12 and delimit a sample volume 17. The distance d which they are spaced apart from each

other typically amounts to from about 0 μm to about 3 cm, most preferably to about 3 mm, wherein the value 0 indicates that the supply and drain ports are located opposite each other. The channel piece 12 communicates with a reservoir R and a waste receptacle W for the electrolyte buffer. The supply channel 13 is connected with a source receptacle S for the sample, while the drain channel 14 communicates with a drain receptacle D.

On page 9, please replace the paragraph starting on line 16 with the following:

The sampling device 3 is part of an electrophoretic chemical ~~anlysis~~analysis system and basically functions in the same way as the sampling device depicted in Fig. 3. However, in order to allow the electrolyte buffer to advance into the supply and drain channels 13, 14 the resistance of flow within the two channels is reduced. In particular the source channel and the drain channel each have a resistance to flow with respect to said electrolyte buffer, which is about 5% lower than the respective resistance to flow of said electrolyte channel. Surprisingly the reduction of the resistance to flow of the supply and drain channels 13, 14 does not result in an increase of the leakage or diffusion of sample components into the electrolyte buffer as it is transported past the respective supply and drain port 15, 16. Instead, the reduction of the resistance to flow of the side channels 13, 14 leads to a convective flow of the electrolyte buffer into the channels 13, 14, even when the ~~aplied~~applied electric fields should not result in such a flow. Thus, the leakage or diffusion of sample components is considerably decreased and the noise of the detected signal is reduced. In consequence the sensitivity of the analytic system, that is the limit of detection, is increased. The resistance to flow of the supply and drain channel can be ~~deminished~~diminished by either reducing the length of the respective channels or by increasing their respective widths w. Preferably the reduction of the resistance to flow of the supply and drain channels 13, 14 is achieved by providing them each with a width w that is at least about two times greater than the width p of the supply and drain ports 15, 16. Such, the supply and drain channels 13, 14 each have about the shape of a bottle, the bottle neck being the respective supply or drain port 15, 16.

On page 10, please replace the paragraph starting on line 1 with the following:

While it is possible that the supply and drain channels 13, 14 empty directly into the channel piece 12 such, that their ends, which are located right next to the channels piece 12 are the respective source and drain ports 15, 16, from where the width of the channels gradually increases over a respective intermediate piece 13', 14' from the width p of the ports to the final width w of the channels, the supply and drain ports also have longitudinal extensions 1. These longitudinal extensions correspond at least to the width p of the respective supply and drain ports 15, 16. It is advantageous, if the widths p of the supply and drain port 15, 16 are kept constant along their longitudinal extension 1. In a preferred embodiment the widths p of the supply and drain port 15, 16 are chosen such, that they about correspond to the width b of the channel piece 12.

On page 10, please replace the paragraph starting on line 17 with the following:

The sampling device 3 according to the invention has been explained with reference to exemplary embodiments which are part of micro-analysis chips. It can as well be an arrangement of capillary tubes, which is part of an electrophoretic chemical analysis system made of capillary tubes. In the most preferred embodiment, however, the sampling device is integrated into a system of capillary channels which are established in a small planar sheet of glass, semiconductor material, or a suitable polymer. Advantageously the channel system including the supply and drain channels and the respective supply and drain ports are etched or micromachined or casted (in case of a polymer base part), or otherwise established in the planar substrate. Most suitable for its manufacture are techniques which are well established in semiconductor production or in the manufacture of micromechanical elements.

On page 10, please replace the paragraph starting on line 33 with the following:

The combination of a structure that geometrically defines the injected sample volume with an electro-kinetic injection of the sample over a defined minimum time period allows to ~~relyably~~reliably control the sample volume and to assure that the composition of the sample contained within the sample volume reflects the original composition of the sample in the reservoir. A further improvement of the method and the sampling device according to the invention allows a considerable reduction of uncontrolled leakage or diffusion of sample components into the electrolyte buffer. Thus, it is possible to reduce the leakage or diffusion such, that the still occurring leakage results in a concentration of the sample in the electrolyte buffer, that is less than 3% of the original concentration of the sample. By this measure the noise of the detected electrophoretic signal is reduced and the detection limits are increased

Please replace the Abstract on page 15 with the following:

~~In a method~~A microfluidic device for controlling sample introduction in microcolumn separation techniques, more particularly in capillary electrophoresis (CRE), where a sample is injected as a sample plug into a sampling device which comprises at least a channel for the electrolyte buffer and a supply and drain channel for the sample. The supply and drain channels discharge into the electrolyte channel at respective supply and drain ports. The distance between the supply port and the drain port geometrically defines a sample volume. The injection of the sample plug into the electrolyte channel is accomplished electrokinetically by applying an electric field across the supply and drain channels for a time at least long enough that the sample component having the lowest electrophoretic mobility is contained within the geometrically defined volume. ~~The supply and drain channels each are inclined to the electrolyte channel.~~ Means are provided for electrokinetically injecting the sample into the sample volume. ~~The resistance to flow of the source and drain channels with respect to the electrolyte buffer is at least about 5% lower than the respective resistance to flow of the electrolyte channel.~~